REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 13, 20 and 21 have been amended to more particularly point out and distinctly claim the subject matter of this invention. The claims have been amended to require that the claimed labeled protein is a protein synthesized in a cell-free protein synthesis system or in a living cell in the presence of the labeling compound, and further that the acceptor portion of the labeling compound excludes a nucleic acid containing a gene. Minor clerical errors have been effected to claim 22.

The support for the limitation that the protein is a protein translated in the presence of the labeling compound is the description of page 13, lines 2-14 of the present specification.

The support for the limitation that the labeling compound excludes the nucleic acid containing the gene is the description of page 17, lines 16-23 of the present specification. From the description, it is clear that the labeling compound naturally excludes the nucleic acid containing the gene. If the labeling compound comprises the nucleic acid containing the gene, the step of adding the nucleic acid containing the gene would become meaningless. Indeed, In Example 1 <3> (b) described in the present specification, 1 μg of plasmid (nucleic acid containing a gene) was added to a protein synthesis system in which Fluorpur or Fluorthiopur (labeling compound) was present (page 27, lines 3-16). When the produced proteins were separated by SDS-PAGE and detected by fluorescence, fluorescent bands were detected at the position corresponding to the original molecular weight of the protein (page 27, line 18 to page 28, line 5), which indicated that the labeled protein did not contain the nucleic acid containing the gene. The amendment is just clarification of inherently disclosed matter.

No new matter is believed to be introduced.

The labeled protein as claimed in the amended claim 13 comprises a protein portion and a labeling compound chemically linked to a C-terminal of the protein portion. The labeling compound comprises an acceptor portion (i.e., puromycin, puromycin analogue) and a label

substance. The protein portion is synthesized in a cell-free protein synthesis system or in a living cell. The acceptor portion excludes a nucleic acid containing a gene.

Claims 13-15 and 20-22 have been rejected under 35 U.S.C. 102(b) as being anticipated by Vince et al. (Biochemistry, 17, 5489-5493 (1978)).

In the response filed March 3, 2003, it was argued as follows:

> "On the contrary, the labeled protein of the present invention is one which comprises a protein portion and a labeling compound chemically linked to a C-terminal of the protein portion.
>
> The labeled protein of the present invention is different from the labeled ribosome obtained by the method of Vince et al. because the analogue is not linked to the C-terminal of the ribosome." (page 2, lines 17-21)

In the outstanding Office Action, the Examiner has stated as follows:

> "Applicants argue that the labeled protein of the invention is different from the labeled ribosome obtained Vince because the puromycin analogue of Vince et al. is not linked to the C-terminal terminal of the ribosome. It is presumed that by this argument applicants are assuming the ribosome was intended by the examiner to meet the 'protein portion' of the labeled protein of Claims 13-15 and 20. This is not persuasive because in fact it is AC[^{14}C]Phe and not the ribosome which is the 'protein portion' of the labeled protein produced by Vince et al." (page 2, the third line from the bottom to page 3, line 6)

Assuming that the ribosome was intended by the Examiner to mean the protein portion, the Applicant gave the explanation about the differences between the present invention and Vince et al. in the previous response. In view of the above statement of the Examiner, the Applicants re-explain about that as follows:

Vince et al. disclose a photoaffinity labeling method of the peptidyl transferase A site of ribosome, and the labeling is based on the radioactive label originated in [^{14}C]Phe (page 5489, abstract). The method is performed in the two-step process as described on page 5491, left

column, lines 20-34 and in Figure 3. For more details, it is described in the Experimental Section (page 5489, right column to page 5491, right column).

First, a mixture of washed ribosomes and NAP-Lys-Pan was incubated and photolyzed. The puromycin moiety contained in NAP-Lys-Pan occupies the A site of ribosome because it resembles the structure of aminoacyl tRNA (Fig. 3-a). By photolyzing it, NAP-Lys-Pan bound to the A site by a covalent linkage (Fig. 3-b). The NAP-Lys-Pan unbound to the A site was removed from the reaction mixture by dialysis.

Second, a mixture of photolyzed ribosomes wherein NAP-Lys-Pan was bound to A sites of the ribosomes, poly(U), Ac[^{14}C]-L-Phe-tRNA, and factors washable from ribosomes (FWR) is incubated. By the poly(U), Ac[^{14}C]-L-Phe-tRNA is directed to the P site of photolyzed ribosome (Fig. 3-c). Transpeptidation of the peptidyl tRNA at the P site subsequently occurs resulting in ^{14}C labeling of the A site (Fig. 3-d).

In this reaction system, if Ac[^{14}C]-L-Phe-tRNA is further directed to the P site, transpeptidation of the peptidyl tRNA at the P site does not occur. Thus, in the reaction of Vince et al., two or more amino acids do not bound to the NAP-Lys-Pan at the A site. In addition, in reaction of Vince et al., because washed ribosomes in which NAP-Lys-Pan is covalently bound to the A site are used, usual translation does not occur.

As discussed above, the labeled protein of the present invention as claimed in the amended claim 13 comprises a protein portion and a labeling compound chemically linked to a C-terminal of the protein portion, wherein the protein portion is synthesized in a cell-free protein synthesis system or in a living cell. Vince et al. are quite silent about a protein synthesis system or in a living cell in the presence of the labeling compound.

Also, the Examiner states that Ac[^{14}C]Phe of the Vince et al. molecule corresponds to the protein portion of the claimed labeled protein. This position is untenable. At a minimum, a protein is composed of two or more amino acids bound by peptide linkage. One amino acid is not a protein.

The labeled protein as claimed in the amended claim 13 and claims depending therefrom is clearly distinguishable and unexpected from the molecule disclosed by Vince et al.

The rejection should be reconsidered and withdrawn.

Claims 13-22 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Nemoto et al. (FEBS Letters, 414, 405-408 (1977)) in view of Promega Technical Bulletin No. 182.

In the amended claims, the labeling compound excludes a nucleic acid comprising a gene. Nemoto et al. are silent about the use of the labeling compound excluding the nucleic acid containing the gene.

Promega Technical Bulletin merely discloses replacement of incorporation of ^{35}S-labeled methionine with incorporation of biotinylated lysine, as seen from Fig. 2 on page 2. Promega does not remedy the basic inadequacy of Nemoto et al. to make the present invention obvious.

The rejection should be reconsidered and withdrawn.

In view of the foregoing, favorable reconsideration and allowance is respectfully solicited.

Respectfully submitted,

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